

NAMANGAN DAVLAT
UNIVERSITETI
ILMIY AXBOROTNOMASI, [2026-9]
ISSN:2181-1458
ISSN:2181-0427



02.00.00-KIMYO FANLARI
journal.namdu.uz
CHEMICAL SCIENCES

UO' K 004.94(544.169)

**AutoDock VINA DASTURI YORDAMIDA MUSKAT YONG' OG' I EFIR MOYI TARKIMIDAGI
BIRIKMALARINING TANLANGAN NISHON OQSILLARI BILAN MULTIPROTEIN DOKING TADQIQOTLARI**

Alisher Gulumbayevich Yeshimbetov

Akad. O.S. Sodiqov nomidagi Bioorganik kimyo instituti

E-mail: ealisherg@yahoo.com

<https://orcid.org/0000-0002-9447-9133>

Annotatsiya: Mazkur ishda muallif tomonidan tuzilgan "Ligand-Multiprotein" yordamchi dasturidan foydalanib, muskat yangogi efir moyi tarkibidagi birikmalarning tanlangan oqsillarga bog' lanish energiyalari AutoDock Vina dasturida o' rganildi. Ligand-Multiprotein yordamchi dasturi bitta ligand molekulasining ketma-ket 55ta va undan ortiq oqsillarga bog' lanish energiyalarini AutoDock Vina dasturi yordamida aniqlash imkonini beradi. Multiprotein tadqiqotlari natijasida muskat yang' og' i efir moyining asosiy tarkib birikmalari 55ta oqsilning ko' pchiligi bilan kuchsiz (>-6 kkal/mol) va o' rtacha ($-6.0 - -8.0$ kkal/mol) bog' lanish energiyalariga ega ekanligi aniqlandi. Ammo, muskat yang' og' i efir moyi tarkibida kam miqdorda uchraydigan ba'zi birikmalar saraton va atsetilxolinesteraza nishon oqsillari bilan kuchli ($-8.0 - -10$ kkal/mol) bog' lanishi aniqlandi. Olingan natijalar muskat yong' og' i efir moyining minor birikmalari uning biologik faolligiga hissa qo' shishi mumkinligini va qo' shimcha ravishda molekulyar dinamik va farmakologik tadqiqotlar o' tkazishni talab qilishini ko' rsatadi.

Kalit so' zlar: Muskat yong' og' i, efir moyi, multiprotein doking, AutoDock Vina

**МУЛЬТИТАРГЕТНЫЙ МОЛЕКУЛЯРНЫЙ ДОКИНГ СОЕДИНЕНИЙ ЭФИРНОГО МАСЛА МУСКАТНОГО
ОРЕХА С ИЗБРАННЫМИ БЕЛКАМИ-МИШЕНЯМИ С ИСПОЛЬЗОВАНИЕМ ПРОГРАММНОГО
ОБЕСПЕЧЕНИЯ AUTODOCK VINA**

Аннотация: В данном исследовании с использованием программы *AutoDock Vina* и разработанной авторами утилиты «*Ligand-Multiprotein*» изучены энергии связывания соединений эфирного масла мускатного ореха с выбранными белками-мишенями. Данная утилита позволяет последовательно определять энергии связывания одной молекулы лиганда с 55 и более белками с использованием *AutoDock Vina*. Многобелковый докинг-анализ показал, что основные компоненты эфирного масла мускатного ореха, как правило, демонстрируют слабое ($> -6,0$ ккал/моль) или умеренное (от $-6,0$ до $-8,0$ ккал/моль) прогнозируемое сродство к большинству из 55 белковых мишеней. Однако несколько соединений, присутствующих в эфирном масле мускатного ореха в относительно низких концентрациях, продемонстрировали сильное прогнозируемое сродство (от $-8,0$ до $-10,0$ ккал/моль) к отдельным мишеням, связанным с онкологическими заболеваниями, а также к ацетилхолинэстеразе (АХЭ). Полученные результаты позволяют предположить, что минорные компоненты эфирного масла мускатного ореха могут вносить вклад в его потенциальную биологическую активность и заслуживают дальнейшего изучения с использованием моделирования молекулярной динамики и экспериментальных методов.

Ключевые слова: Мускатный орех, эфирные масла, мультипротеиновая стыковка, *AutoDock Vina*

**MULTITARGET MOLECULAR DOCKING ANALYSIS OF NUTMEG ESSENTIAL OIL COMPOUNDS AGAINST
SELECTED PROTEIN TARGETS USING AUTODOCK VINA SOFTWARE**

Abstract: In this study, the binding energies of nutmeg essential oil compounds with selected protein targets were investigated using the *AutoDock Vina* program and the author-developed "Ligand-Multiprotein" utility. This utility enables the sequential determination of the binding energies of a single ligand molecule against 55 or more proteins using *AutoDock Vina*. Multiprotein docking analysis showed that the major constituents of nutmeg essential oil generally exhibited weak (> -6.0 kcal/mol) to moderate (-6.0 to -8.0 kcal/mol) binding affinities toward most of the 55 protein targets. However, several compounds present in nutmeg essential oil at relatively low concentrations demonstrated strong predicted binding affinities (-8.0 to -10.0 kcal/mol) toward selected cancer-related and acetylcholinesterase (AChE) targets. These findings suggest that minor constituents of nutmeg essential oil may contribute to its potential biological activity and warrant further investigation using molecular dynamics simulations and experimental studies.

Keywords: Nutmeg, essential oils, multiprotein docking, *AutoDock Vina*

Kirish

Keyingi yillarda olimlar tomonidan ziravorlarning kimyoviy tarkibi va undagi asosiy hamda minor tarkib birikmalarining farmakologik tadqiqotlari keng o'rganilmoqda. Yurimizga chet davlatlardan import qilinadigan ziravorlardan biri - muskat yong'og' idir (*Myristica fragrans*). Muskat yong'og' i efir moyi kosmetika sanoatida tabiiy xushbo' yashtiruvchi vosita va atir sifatida ishlatiladi [1]. Undan tashqari uning mikroblarga qarshi va antioksidant faolligi haqida ma'lumotlar mavjud [1]. Muskat yong'og' i efir moylari tarkibiga kiruvchi birikmalarni multiprotein molekulyar doking usulida tadqiq qilish "Ligand-Multiprotein [2]" uslubini baholash, takomillashtirish hamda dasturga kiritilgan nishon oqsillarining ishonchliligini oshirishi mumkin.

Adabiyotlar sharxi

Ma'lumki, o' simliklar va ulardan olinadigan yog' larning kimyoviy tarkibi ularning turi va yetishtiriladigan mintaqasiga qarab turlicha nisbatda bo'lishi mumkin [3]. Masalan, Nigeriya olimlari muskat yong'og' i yog' ining asosiy tarkib birikmalari sifatida sabinen (49.09%), α -pinen (13.19%), α -fellandren (6.72%) va terpinen-4-ol (6.43%) birikmalari ekanligini GC-MS tahlillari asosida keltirishgan [4] bo'lsa, Indoneziyalik olimlar xuddi shu usulni qo'llagan holda quyidagi tarkibni keltirishgan: sabinen (21.4%), α -pinen (10.2%), miristitsin (10.6%), terpinen-4-ol (13.9%), safrol (4.3%), γ -terpinen (4.0%) [5]. Pokistonlik olimlar esa quyidagi tarkibni keltirishgan [6]: sabinen (18.9%), α -pinen (15.8%), simen (15.2%), terpinen-4-ol (11.7%), elemitsin (11.5%) va safrol (6.2%).

Hindistonlik olimlar mamlakatning turli mintaqalarida yetishtiriladigan muskat osimligi urug' i (muskat yang'og' i) efir moylari tarkibi bir-biridan farq qilishini aniqlashgan [3]. Andaman va Nikobar orollaridan olingan muskat yang'og' i tarkibi miristitsin (20.3%), sabinen (19.3%), α -tuyen (12.1%), α -pinen (9.5%), terpinen-4-ol (7.1%), limonene (5.9%), γ -terpinen (4.1%), elemitsin (4.0%) birikmalaridan iborat [7] bo'lsa, Hindiston g' arbiy qismlarida yetishtirilgan muskat yang'og' i efir moyi tarkibi sabinen (27.7%), α -pinen (21.8%), β -pinen (18.2%), limonen (6.4%) va β -mirsen (2.9%) ekanligi topilgan [8].

Muskat yang'og' i efir moyi tarkibiga kiruvchi birikmalarining AutoDock Vina dasturida [9] molekulyar doking tadqiqotlari muskat va uning efir moylari haqida to'liqroq ma'lumotlar olishimizga va ular haqidagi bilimlarimizning oshishiga olib kelishi mumkin. Shundan kelib chiqqan holda, ushbu maqolada muskat yang'og' i efir moyi tarkibida uchraydigan birikmalarning har birining 55ta oqsil molekullari bilan ta'sirlashishlari "Ligand-Multiprotein" yordamchi dasturida o'rganildi.

Tadqiqot metodologiyasi

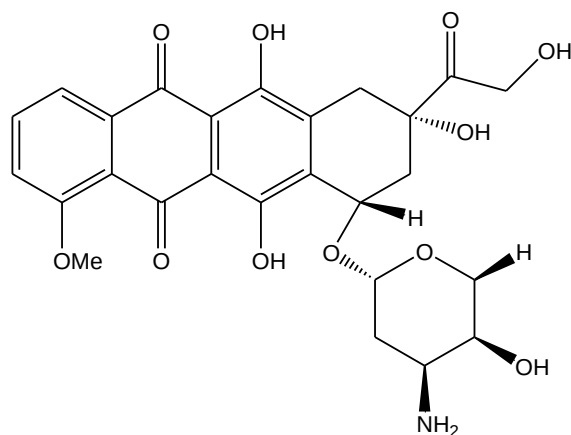
Ushbu tadqiqotda ChatGPT yordamida Perl algoritmi tilida tuzilgan "Ligand-Multiprotein (vina_multi.pl)" yordamchi dasturi va AutoDock Vina [9] dasturi multiprotein tadqiqotlari uchun qo'llanildi. Dastlabki dasturga kiritilgan oqsillar soni 30tadan 55taga yetkazildi. Dastlab oqsil molekullari oqsillar ma'lumotlar bazasidan (Protein Data Bank-PDB, <https://www.rcsb.org/> [10]) pdb fayl ko'rinishida yuklab olindi. Keyin, AutoDockTools-1.5.7 [11] dasturida pdbqt faylga o'girildi. Oqsillar faol markazlari CB-Dock2 serverida [12] aniqlandi va ular har bir oqsil uchun tuzilgan config(*).txt fayllarida aks ettirildi.

Ligand molekullari PubChem (<https://pubchem.ncbi.nlm.nih.gov/>) bazasidan sdf fayl ko'rinishida yuklab olinib, Biovia DS visualizer dasturida (Dassault Systemes BIOVIA, USA) pdb faylga o'girildi. Har bitta ligand molekulasi doking tadqiqotidan oldin LIG.pdbqt fayli ko'rinishida saqlandi.

Natijalar va ularning tahlillari

Ma'lumki, AutoDock Vina dasturida doking tadqiqotlari Windows buyruqlar satri orqali amalga oshiriladi. Shu sababli, Perl algoritmi tilida tuzilgan "Ligand-Multiprotein (vina_multi.pl)" yordamchi dasturi ham buyruqlar satrida bajariladi: "C:/perl vina_multi.pl" buyrug' i orqali AutoDock Vina dasturiga ketma-ket bitta ligandning (LIG.pdbqt) turli oqsillar (55ta) bilan ta'sirlashishini o'rganishga buyruq beradi va natijada umumiy LIG-Oqsillar (multiprotein) doking tadqiqotining amalga oshirilishini ta'minlaydi. Doking jarayonida config(*).txt fayli muhim o'rin tutadi va unda oqsil (retseptor) nomi, faol markazi koordinatalari (X, Y, Z) hamda faol markaz o'lchami ($X=Y=Z=\text{\AA}$) keltiriladi. Natijalar 55ta out*.pdbqt (yulduzcha o'rinda oqsil nomi yoki kodi) fayl ko'rinishida paydo bo'ladi.

Oldin [2] ta'kidlanganidek, multiprotein doking dasturida bitta kasallik uchun javobgar bir nechta oqsillar inobatga olingan. Masalan, saraton kasalligi uchun olingan nishon oqsillari soni 23ta. Dastlab, ularning saraton amaliyotida qo'llaniladigan doksorubitsin (doxorubicin [13]) dori vositasi bilan ta'sirlashish energiyasi aniqlandi. Doksorubitsin 23ta nishon oqsillarining 14tasi bilan $BE=-8.0 \div -11.0$ kkal/mol bog'lanish energiyasini hosil qilgan bo'lsa, yana 8tasi bilan $BE=-6.7 \div -7.8$ kkal/mol ekanligi topildi. Qolgan bitta oqsil bilan nisbatan kuchsiz bog'lanish kuzatilishi aniqlandi: 1GFW ($BE=-5.5$ kkal/mol). Eng mustahkam bog'lanish 3GHW (DHFR) oqsili ($BE=-11.0$ kkal/mol) bilan kuzatildi.

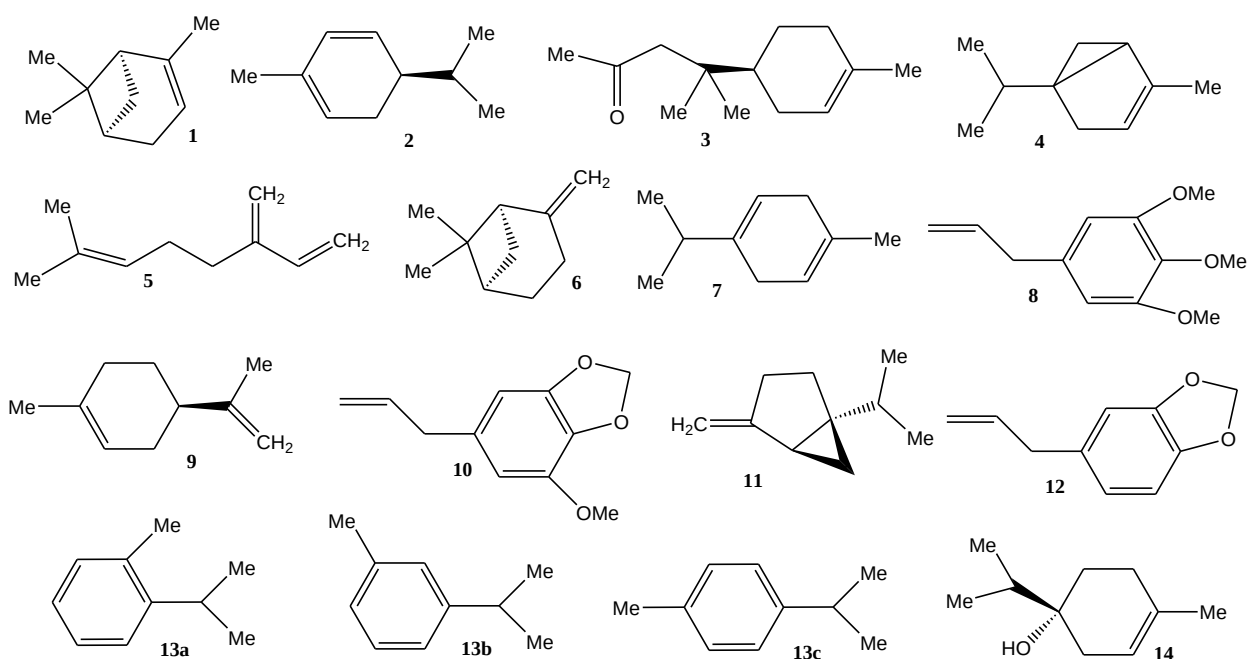


1-rasm. Dokso-rubitsinning tuzilish formulasi.

Demak, bironta ligand molekulasining ushbu (23ta) oqsillarning kamida 60% bilan mustahkam ta'sirlashishi, ya'ni bog'lanish energiyasi $BE = -8.0 \div -10.0$ kkal/mol kuzatilsa, ayni ligandning saratonga qarshi faollikka ega dori vositasi bo'lishi mumkinligini ko'rsatadi.

Tabiiy birikmalar o'ziga xos tuzilishi va kutilmagan biologik faolliklari bilan ko'pchilik olimlar e'tiborini tortib kelmoqda. Muskat yong'og'i efir moyi asosan monoterpen va seskviterpen birikmalaridan iborat bo'lib, efir moyi biologik xususiyatlariga katta hissa qo'shadi. Ular tarkibidagi birikmalarni molekulyar doking usulida 55ta oqsil molekulalari bilan bog'lanishlarini tadqiq qilish orqali skrining qilish "Ligand-Multiprotein" yordamchi dasturini mukammallashtirishi va ziravorlarning kundalik hayotdagi tadbigi bo'yicha foydali ma'lumotlar yig'ilishiga sabab bo'lishi mumkin.

Muskat yang'og'i efir moyi tarkibiga kiruvchi asosiy (tarkibida ko'proq miqdorda uchraydigan) birikmalar 2-rasmda keltirilgan. Unda Grenada orolida yetishtiriladigan muskat yangogi efir moyi tarkibida uchraydigan α -terpinil atsetat [14] ham kiritilgan. Adabiyotlarda [3-8] simen (cymene, 13) birikmasining qaysi biri ekanligi yozilmagan, shuning uchun uchta, ya'ni *orto*-, *meta*- va *para*-simenlar inobatga olindi. Ligand-Multiprotein doking tadqiqotlari natijalari 1 va 2-jadvalda keltirilgan. Unga ko'ra, muskat yang'og'i efir moyining asosiy tarkib birikmalari 55ta oqsilning ko'pchiligi bilan kuchsiz (>-6 kkal/mol) bog'lanadi. Ba'zilar bilan esa o'rtacha ($-6.0 \div -8.0$ kkal/mol) BE orqali bog'lanadi.



2-rasm. Muskat yang'og'i efir moyining asosiy tarkib birikmalari. 1) α -pinen; 2) α -fellandren; 3) α -terpinil atsetat; 4) α -tuyen; 5) β -mirsen; 6) β -pinen; 7) γ -terpinen; 8) Elemitsin; 9) Limonen; 10) Miristitsin; 11) Sabinen; 12) Safrol; 13a) o-Simen; 13b) m-Simen; 13c) p-Simen va 14) Terpinen-4-ol.

Jadval 1

Muskat yang'og'i efir moyining asosiy tarkib birikmalari va 55ta oqsillar bilan bog'lanish energiyalari (BE) oralig'i

No	Birikma	BE oralig'i, kkal/mol
1	α -pinen α -pinene	$-3.5 \div -7.0$

2	α -felandren	α -phellandrene	-4.0 ÷ -7.5
3	α -terpinil atsetat	α -terpinyl acetate	-4.4 ÷ -8.0
4	α -tuyen	α -thujene	-3.9 ÷ -7.3
5	β -mirsen	β -myrcene	-3.1 ÷ -6.6
6	β -pinen	β -pinene	-3.5 ÷ -6.9
7	γ -terpinen	γ -terpinene	-3.6 ÷ -7.6
8	Elemitsin	Elemicin	-4.5 ÷ -7.1
9	Limonen	Limonene	-3.8 ÷ -7.4
10	Miristitsin	Myristicin	-4.5 ÷ -7.6
11	Sabinen	(-)-Sabinene	-3.8 ÷ -6.9
12	Safrol	Safrole	-4.1 ÷ -7.6
13a	o-Simen	o-Cymene	-3.8 ÷ -7.4
13b	m-Simen	m-Cymene	-3.9 ÷ -7.6
13c	p-Simen	p-Cymene	-3.6 ÷ -7.6
14	Terpinen-4-ol	Terpinen-4-ol	-4.0 ÷ -7.1

Muskat yang' og' i efir moyi tarkibiga ko' p miqdorda uchraydigan sabinen (11) birikmasi butuirilxolinesteraza (BXE) nishon oqsili 7QHD bilan ta'sirlashish energiyasi -6.8 kkal/mol ekanligi aniqlandi. Suningdek, sabinen saraton turlaru uchun nishon oqsili sifatida kiritilgan 2HZI, 4Y83 va 2X7F oqsillari bilan mos ravishda -6.8, -6.8 va -6.9 kkal/mol bog' lanishga ega ekanligi topildi. Ko' pchilik muskat yang' og' i turlari efir moylarini tarkibida sabinendan keyingi o' rinda ko' proq miqdorni tashkil qiladigan α -pinen faqat ikkita oqsil bilan (2UV0 va 2X7F) o' rtacha bog' lanish energiyasiga (BE=-7.0 kkal/mol) ega. 2UV0 oqsili *P. aeruginosa* bakteriyasining nishon oqsili hisoblanadi [15]. 2X7F oqsili esa yo' g' on ichak saratoniga qarshi dori vositalarini topishda keng qo' llaniladigan nishon oqsili hisoblanadi [16].

P. aeruginosa bakteriyasining boshqa bir nishon oqsili (PDB ID: 7OC1 [17]) bilan miristitsin (10) birikmasining α -pinenga nisbatan mustahkamroq (BE=-7.5 kkal/mol) bog' lanishi doking tadqiqotlari natijasida aniqlandi. Shuningdek, miristitsin (10) birikmasi atsetilxolinesteraza (AXE) fermenti nishon oqsili 4M0E [18] (BE=-7.4 kkal/mol) va saraton nishon oqsillari 2E2B [19] va 6LZL [20] bilan BE=-7.6 kkal/mol bog' lanish energiyasiga ega. Saraton kasalligiga javobgar sifatida dasturga kiritilgan 2E2B, 2HZI va 2X7F nishon oqsillari [19] bilan eng mustahkam bog' lanishni Grenada orolida yetishtiriladigan muskat yang' og' i efir moyi tarkibida uchraydigan α -terpinil atsetat (3) birikmasi uchun kuzatildi.

α -Felandren (2), α -tuyen (4), β -mirsen (5), β -pinen (6) va limonen (9) birikmalarining eng kuchli boglanish energiyalari saraton oqsillari bilan ekanligi aniqlandi. γ -Terpinen (7), elemitsin (8) va o-simen birikmalari AXE va saraton oqsillariga qariyb bir xil bog' lanish energiyasiga ega. Bu holat m-simen va p-simen birikmalari uchun ham xosdir. Qo' shimcha ravishda ular (m-simen va p-simen) *P. aeruginosa* bakteriyasi 2UV0 oqsiliga qariyb bir xil bog' lanish energiyasiga ega. Tuzilish jihatidan bir xil bo' lgan miristitsin (10) va safrol (12) birikmalarining saraton nishon oqsillariga bog' lanish energiyalari bir xil bo' lib, miristitsindagi -OMe guruhi oqsil-ligand ta'sirlashish energiyasida sezilarli o' zgarishni yuzaga keltirmagan (2-jadval).

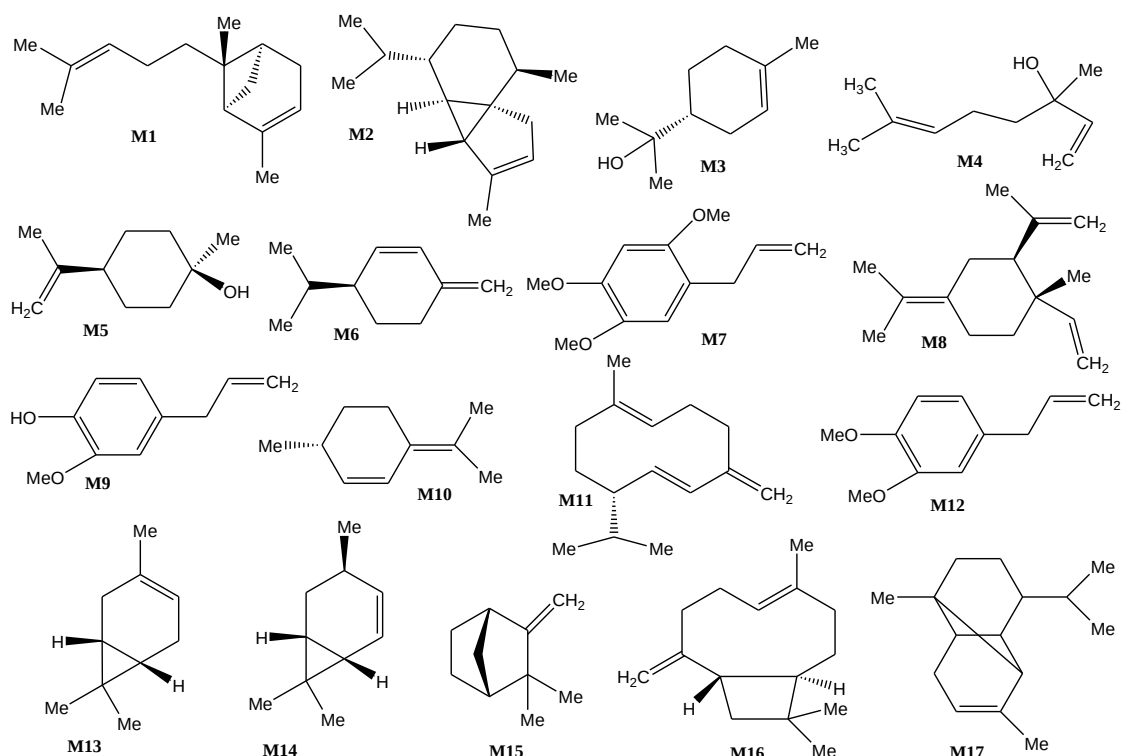
Muskat yang' og' i efir moyi tarkibidagi kam miqdorda uchraydigan (minor) birikmalar va ularning oqsillar bilan ta'sirlashish energiyalari ham katta ahamiyat kasb qiladi. Ularning efir moydagi ulushi bir foizdan kam [3]. Ularning tuzilish formulalari 3-rasmda keltirilgan. Multiprotein doking natijalarida aniqlangan BE oralig' i 3-jadvalda keltirilgan. Undan α -Bergamoten (M1) va α -Kubeben (M2) seskviterpen birikmalari uchun juda yaxshi natija aniqlandi. M1 birikma 4ta saraton oqsillari va bitta AXE fermenti bilan mustahkam bog' lanish hosil qildi. Adabiyotlarda uning saratonga qarshi faolligi haqida ma'lumotlar bor [21]. M2 birikmasi esa eng mustahkam bog' lanishni AXE fermenti (1DX6) bilan hosil qildi (4-jadval).

Jadval 2

Doking natijasida aniqlangan muskat yang' og' i efir moyining asosiy tarkib birikmalarining eng yaxshi bog' lanishlari

No	Birikma	PDB ID (BE, kkal/mol)
1	α -Pinen	2UV0 (-7.0), 2X7F (-7.0)
2	α -Felandren	2E2B (-7.5)
3	α -Terpinil atsetat	2UV0 (-7.7), 4M0E (-7.7), 2HZI (-7.9), 2X7F (-7.9), 2E2B (-8.0)
4	α -Tuyen	2E2B (-7.3), 2X7F (-7.3)
5	β -Mirsen	2X7F (-6.5), 2E2B (-6.6)
6	β -Pinen	2HZI (-6.9)

7	γ-Terpinen	2E2B (-7.6), 4M0E (-7.6)
8	Elemitsin	4M0E (-7.0), 2E2B (-7.1)
9	Limonen	2X7F (-7.2), 2E2B (-7.4)
10	Miristitsin	4M0E (-7.4), 7OC1 (-7.5), 2E2B (-7.6), 6LZL (-7.6)
11	Sabinen	7QHD (-6.8), 2HZI (-6.8), 4Y83 (-6.8), 2X7F (-6.9)
12	Safrol	7QHD (-7.5), 4Y83 (-7.5), 2E2B (-7.6), 2UV0 (-7.6), 6LZL (-7.6)
13a	o-Simen	4M0E (-7.3), 2E2B (-7.4)
13b	m-Simen	2UV0 (-7.3), 4Y83 (-7.4), 4M0E (-7.5), 2E2B (-7.6)
13c	p-Simen	2UV0 (-7.2), 4Y83 (-7.2), 6LZL (-7.3), 4M0E (-7.6), 2E2B (-7.6)
14	Terpinen-4-ol	2X7F (-7.1), 3TZM (-7.1)



3-rasm. Muskat yang' og' i efir moyining minor tarkib birikmalari

Jadval 3

Muskat yang' og' i efir moyining minor birikmalari va 55ta oqsillar bilan bog' lanish energiyalari (BE) oralig' i

No	Birikma		BE oralig' i, kkal/mol
M1	α-Bergamoten	α-Bergamotene	-4.1 ÷ -8.5
M2	α-Kubeben	α-Cubebene	-4.2 ÷ -10.1
M3	α-Terpineol	α-Terpineol	-3.9 ÷ -7.2
M4	β-Linalool	β-Linalool	-3.7 ÷ -6.4
M5	β-Terpineol	β-Terpineol	-3.9 ÷ -7.2
M6	β-Fellandrene	β-Phellandrene	-3.7 ÷ -7.3
M7	γ-Asaron	γ-Asarone	-4.8 ÷ -7.3
M8	γ-Element	γ-Elementene	-4.1 ÷ -8.4
M9	Evgenol	eugenol	-4.0 ÷ -7.1
M10	Izoterpinolen	Isoterpinolene	-4.0 ÷ -7.1
M11	Germacren-D	Germacrene-D	-4.3 ÷ -9.0
M12	Metilevgenol	Methyleugenol	-4.0 ÷ -7.2
M13	3-Karen	3-carene	-3.7 ÷ -7.6
M14	4-Karen	4-carene	-3.6 ÷ -7.4
M15	Kamfen	camphene	-3.4 ÷ -6.7
M16	Kariofillen	caryophyllene	-4.3 ÷ -8.8
M17	Kopaen	copaene	-4.3 ÷ -8.9

Ligand-Multiprotein yordamchi dasturida AXE fermentiga tegishli inson (4M0E) va Tetronarce californica (1DX6) organizmlarida mavjud AXE fermentlari bilan birgalikda BXE (7QHD) fermenti ham kiritilgan. Tibbiyot amaliyotida qo' llaniladigan, AXE fermentlarini qaytar ingibirlovchi galantamin va donepezil dori vositalarining ushbu fermentlarga bog' lanish energiyalari $-9.5 \div -10.5$ kkal/mol [22]. Ilmiy manbalarda M2 moddasining antixolinesteraza faolligi haqida ma'lumotlar yo' q. Ammo, saratonga qarshi faolligi haqida ma'lumotlar mavjud [23]. M2 birikmasi 3EZW (-8.0) va 6LZL (-8.1) saraton oqsillari bilan ham mustahkam bog' lanish hosil qilishi molekulyar doking tadqiqotlari natijasida aniqlandi (4-jadval). Qo' shimcha ravishda M2 birikmasi P. aeruginosa bakteriyasining nishon oqsili (7OC1) bilan BE=-8.1 kkal/mol energiyaga ega mustahkam bog' lanish hosil qilishi topildi. Bu holat farmakologik tadqiqotlarda tarkibida ko' proq miqdorda α -kubeben (M2) tutgan efir moylarining antibakterial faollik natijalari bilan mos tushadi [24]. Undan tashqari, M2 birikmasi 1MWR oqsili bilan mustahkam bog' lanish (-8.4 kkal/mol) hosil qilgan. 1MWR S. aureus bakteriyasining antibiotiklarga bardoshligiga qarshi (antibiotic resistance) qo' llaniladigan nishon oqsili hisoblanadi.

Jadval 4

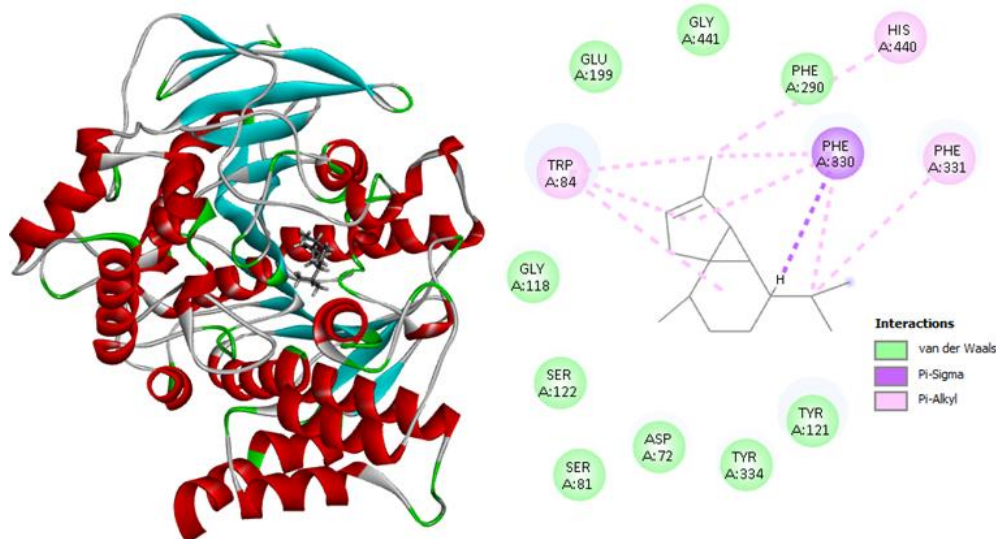
Doking natijasida aniqlangan muskat yang' og' i efir moyining asosiy tarkib birikmalarining eng yaxshi bog' lanishlari

Birikma	PDB ID (BE, kkal/mol)
M1	6LZL (-8.1), 2OH4 (-8.1), 2E2B (-8.2), 4M0E (-8.5), 2HZI (-8.5)
M2	3EZW (-8.0), 7QHD (-8.0), 7OC1 (-8.1), 6LZL (-8.1), 1MWR (-8.4), 4M0E(-8.7), 1DX6 (-10.1)
M3	4Y83 (-7.0), 2X7F (-7.1), 2E2B (-7.2)
M4	1DX6 (-6.3), 7QHD (-6.3), 2E2B (-6.3), 4Y83 (-6.4)
M5	1DX6 (-7.0), 2OH4 (-7.0), 2UV0 (-7.0), 2X7F (-7.2)
M6	1DX6 (-7.0), 2X7F (-7.0), 2E2B (-7.3)
M7	2E2B (-7.0), 4M0E(-7.1), 7OC1 (-7.3)
M8	1MWR (-8.0), 2E2B (-8.1), 2UV0 (-8.3), 1DX6 (-8.4)
M9	4Y83 (-7.0), 2E2B (-7.1)
M10	4Y83 (-7.0), 2E2B (-7.1)
M11	4M0E(-8.0), 3GHW (-8.0), 1MWR (-8.1), 2HZI (-8.3), 1DX6 (-9.0)
M12	7QHD (-7.0), 2UV0 (-7.0), 1DX6 (-7.1), 2E2B (-7.2)
M13	7QHD (-7.0), 2UV0 (-7.2), 2X7F (-7.3), 1DX6 (-7.6)
M14	2UV0 (-7.2), 1DX6 (-7.3), 2X7F (-7.4)
M15	2X7F (-6.6), 1DX6 (-6.6), 2UV0 (-6.7)
M16	2X7F (-8.0), 7QHD (-8.0), 2HZI (-8.1), 4M0E (-8.2), 3GHW (-8.3), 1CM8 (-8.5), 1MWR (-8.6), 1DX6 (-8.6)
M17	4M0E (-8.1), 7QHD (-8.1), 3GHW (-8.4), 1DX6 (-8.7), 1MWR (-8.7), 2HZI (-8.9)

M8, M11, M16 va M17 birikmalar qolgan minor birikmalardan BE kattaligi oralig' i bo' yicha ajralib turishi aniqlandi (3-jadval). Ular AXE fermenti bilan mos ravishda -8.4, -9.0, -8.6 va -8.7 kkal/mol energiya orqali kuchli bog' lanishi aniqlandi. Shuningdek, M8 bitta (2E2B), M11 ikkita (3GHW, 2HZI), M16 to' rta (1CM8, 2X7F, 2HZI va 3GHW) va M17 ikkita (3GHW, 2HZI) saraton oqsillari bilan mustahkam bog' lanishi kuzatildi.

M3-M7, M9, M10, M12-M15 minor birikmalari saraton oqsillari bilan o' rtacha bog' lanishi kuzatildi (4-jadval).

α -Kubeben (M2) birikmasi 1DX6 (AXE) fermenti faol markazida yaxshi joylashib, Trp84, Phe330, Phe331 va His440 aminokislota qoldiqlari bilan π - σ (alkil) ta'sirlashlarni yuzaga keltirishi aniqlandi (4-rasm). Bir tomondan, α -kubeben (M2) birikmasining 1DX6 (AXE) fermentiga bog' lanish energiyasining galantaminning bog' lanish energiyasi kabi bo' lganligi katta qiziqish uyg' otadi. Ammo, ikkinchi tomondan, α -Kubeben-1DX6 kompleksi mustahkamligi haqidagi oxirgi xulosalar suv muhitida olib boriladigan molekulyar dinamik simulyatsiyalardan keyin qilinishi mumkin. Sababi, suv muhitida M2 AXE faol markazidan qisman siljishi yoki butunlay chiqib ketishi mumkin. Shundan kelib chiqqan holda, muskat yang' og' i efir moyi tarkibidagi M2 kabi birikmalarning antixolinesteraza faolligi haqidagi xulosalar in vitro tadqiqotlari natijasida aniqlanishi mumkin.



4-rasm. α -Kubebenning 1DX6 oqsili faol markazida joylashishi (chapda) va uning aminokislota qoldiqlari bilan ta'sirlashishlari (o'ngda)

Xulosa

Bitta ligand molekulasining bir nechta oqsilga ketma-ket, AutoDock Vina dasturida doking qilish imkonini beruvchi "Ligand-Multiprotein (vina_multi.pl)" yordamchi dasturi kichik organik birikmalarning mumkin bo'lgan faollik turlarini yuzaga chiqarishda muhim ahamiyat kasb qilishi mumkin.

Muskat yang'og' i efir moyi tarkibida uchraydigan birikmalarning birontasi ham dasturga kiritilgan 23ta saraton oqsilining 60% qismi bilan kuchli bog'lanish hosil qilmadi. Multiprotein tadqiqotlari natijasida muskat yang'og' i efir moyining asosiy tarkib birikmalari 55ta oqsilning ko'pchiligi bilan kuchsiz (>-6 kkal/mol) va o'rtacha ($-6.0 \div -8.0$ kkal/mol) bog'lanish energiyalariga ega ekanligi aniqlandi. Ammo, muskat yang'og' i efir moyi tarkibida kam miqdorda uchraydigan ba'zi birikmalar saraton va atsetilxolinesteraza nishon oqsillarining bir nechtasi bilan kuchli ($-8.0 \div -10$ kkal/mol) bog'lanishi aniqlandi.

Mutaxassis tadqiqotchi tomonidan bitta ligandning 55ta oqsilga bog'lanish energiyasi PyRx dasturi va CB-Dock2 serverida 1-3 kunda amalga oshiriladigan bo'lsa, "Ligand-Multiprotein (vina_multi.pl)" yordamchi dasturi orqali bir soat vaqt mobaynida amalga oshirilishi mumkin.

Kelajakda, uslubning ahamiyatini yanayam oshirish maqsadida "Ligand-Multiprotein (vina_multi.pl)" yordamchi dasturiga kiritilgan nishon oqsillari sonini ko'paytirish (100taga yetkazish) va biologik faolliklari o'rganilgan birikmalarni doking qilish orqali dasturning ishonchlilik darajasini oshirish orqali usulni takomillashtirish rejalashtirilmoqda.

Muallif(lar) hissasi, manfaatlar to'qnashuvi va moliyalashtirish

AutoDock Vina molekulyar doking dasturi ochiq (bepul) dastur bo'lib, uning asosida pullik dasturlar tuzish dastur yaratuvchilari tomonidan taqiqlangan. Shu sababli "Ligand-Multiprotein (vina_multi.pl)" yordamchi dasturi ham ochiq (bepul) dastur hisoblanadi. Dastur takomillashtirilganidan keyin, u haqida qiziqish bildirgan OTM va ITM xodimlariga taqdim qilinishi mumkin.

Foydalanilgan adabiyotlar

1. Mustafiah M., Kurniawansyah F., Mahfud M. Enhanced extraction of Myristica fragrans houtt seed essential oil via microwave air-hydrodistillation: Parametric study, optimization, and antibacterial evaluation // Results in Engineering. 2026. –Vol. 29. –P.109074
2. Yeshimbetov A.G. AutoDock Vina dasturida kurkumin va piperinlarning multiprotein doking tadqiqotlari// Qoqon DPI. Ilmiy xabarlar jurnali. -2026. –Vol.9.
3. Ashokkumar K., Simal-Gandara J., Murugan M., Dhanya M.K., Pandian A. Nutmeg (Myristica fragrans Houtt.) essential oil: A review on its composition, biological, and pharmacological activities. Phytother. Res. –2022. –Vol.36(7). –P.2839-2851.
4. Ogunwande I.A., Olawore N.O., Adeleke K.A., Ekundayo O. Chemical Composition of Essential Oil of Myristica fragrans Houtt (Nutmeg) From Nigeria. Journal of Essential Oil Bearing Plants. –2003. –Vol.6(1). –P.21–26.
5. Muchtaridi, Subarnas A., Apriyantono A., Mustarichie R. Identification of compounds in the essential oil of nutmeg seeds (Myristica fragrans Houtt.) that inhibit locomotor activity in mice. International Journal of Molecular Sciences. 2010. Vol.11. –P.4771–4781.

6. Muhammad I.S., Mahmood A., Ayesha R., Zahoor Q.S., et al. Chemical composition of the essential oils of nutmeg and mace by GC-FID/MS indigenous to Pakistan and evaluation of their biological activities. *Latin American Journal of Pharmacy*, 2016. 35(10), 2176–2184
7. Waman A. A. Essential oil composition of clove and nutmeg from Andaman and Nicobar Islands, India. *Indian Journal of Biochemistry & Biophysics*, -2020. -Vol.57, -P.95–100
8. Ashokkumar K., Vellaikumar S., Murugan M., Dhanya M.K., Aiswarya S. Compositional variation in the leaf, mace, kernel, and seed essential oil of nutmeg (*Myristica fragrans* Houtt.) from the Western Ghats, India. *Natural Product Research*, -2022. Vol.36(1). -P432–435.
9. Trott O., Olson A.J., AutoDock Vina: Improving the speed and accuracy of docking with a new scoring function, efficient optimization and multithreading // *J. Comput. Chem.* -2010. -Vol.31. -455-461.
10. Kim S., Chen J., Cheng T., Gindulyte A. et al. PubChem 2025 update // *Nucleic Acids Research*. -2025. -Vol.53. -P.1516–1525
11. Morris G.M., Huey R., Lindstrom W., Sanner M.F. et. al. AutoDock4 and AutoDockTools4: Automated docking with selective receptor flexibility // *J. Comput. Chem.* -2009. -Vol.30. -P.2785–2791.
12. Liu Y., Yang X., Gan J., Chen S., Xiao Z.X., Cao Y. CB-Dock2: Improved protein-ligand blind docking by integrating cavity detection, docking and homologous template fitting // *Nucleic Acids Research*. -2022. -50(W1). -W159-W164.
13. Bhadran A., Polara H., Babanyinah G.K., Baburaj S., Stefan M.C. Advances in Doxorubicin Chemotherapy: Emerging Polymeric Nanocarriers for Drug Loading and Delivery // *Cancers*. -2025. -Vol.17(14). -P2303.
14. Mickus R., Jančiukė G., Raškevičius V., Mikalayeva V., et al. The effect of nutmeg essential oil constituents on Novikoff hepatoma cell viability and communication through Cx43 gap junctions // *Biomedicine & Pharmacotherapy*. -2021. -Vol.135. -P.111229.
15. Srinivasarao S., et al. Design, synthesis and biological evaluation of 1,2,3-triazole based 2-aminobenzimidazoles as novel inhibitors of LasR dependent quorum sensing in *Pseudomonas aeruginosa* // *RSC Advances*. -2019. -Vol.9(50). -P.29273–29292.
16. Masuda M., Uno Y., Ohbayashi N., Ohata H., et al. TNIK inhibition abrogates colorectal cancer stemness // *Nat. Commun.* -2016. -Vol.7. -P.12586.
17. Espeland L.O., Georgiou C., Klein R., et al. An Experimental Toolbox for Structure-Based Hit Discovery for *P. aeruginosa* FabF, a Promising Target for Antibiotics // *ChemMedChem*. -2021. -Vol.16. -P. 2715.
18. Cheung J., Gary E.N., Shiomi K., Rosenberry T.L. Structures of Human Acetylcholinesterase Bound to Dihydrotanshinone I and Territre B Show Peripheral Site Flexibility // *ACS Med. Chem. Lett.* -2013. -Vol.4(11). -P.1091–1096.
19. Jha V., Bhosale A., Kapadia P., Bhargava A., Marick A., Charania Z., Parulekar O., Shaikh M., Madaye B. Multitargeted molecular docking study of phytochemicals on hepatocellular carcinoma // *J. App. Biol. Biotech.* -2023. -Vol.11(1). -P.116–130.
20. McLean L.R., Zhang Y., Degnen W., Peppard J. Discovery of novel inhibitors for DHODH via virtual screening and X-ray crystallographic structures // *Bioorg. Med. Chem. Lett.* -2010. -Vol.20(6). -P.1981–1984
21. Annaz H., El Fakhouri K., Ben Bakrim W., Mahdi I., et al. Bergamotenes: A comprehensive compile of their natural occurrence, biosynthesis, toxicity, therapeutic merits and agricultural applications // *Crit. Rev. Food Sci. Nutr.* -2024. -Vol.64(21). -P.7343–7362.
22. Eshimbetov A., Rasulov A., Palvanov N., Kudiyarova A., Ashurov J., Ibragimov B. Molecular docking and molecular dynamics analysis of selected anticholinesterase inhibitors from the ZINC database // *New Mater. Compd. Appl.* -2026. -Vol.10. -N1. -P.105–120.
23. Boualam K., Ortaakarsu A.B., Khatib S., et al. Bibliometric Analysis of Cubebenes and Related Sesquiterpenes: Natural Occurrence, Biosynthesis, Pharmacological Activities, and In-Silico-Based Future Therapeutic Potential // *eFood*. -2026. -Vol.7. -e70128.
24. Sreepian P.M., Popruk S., Rattanasinganchan P., Sreepian A. Comprehensive investigation of *Litsea cubeba* antibacterial and antifungal activities across solid, liquid, and vapor phases against key human pathogens // *Narra J.* -2025. -Vol.5(1). -e1685.